REMARKS/ARGUMENTS

In response to the final Office Action dated August 3, 2007, Applicants have amended the claims which when considered with the following remarks, is deemed to place the present application in condition for allowance. Favorable consideration of all pending claims is respectfully requested.

In order to advance prosecution in this application, claim 12 has been amended to recite in relevant part: "wherein less than 5% of oils apart from those present in the surfactant, are present in the composition" rather than "the composition being substantially free of any additional oil." Claim 25 has been canceled without prejudice. Support for this amendment may be found throughout the specification, e.g., page 2, lines 10-11.

Claims 12-26 remain rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-9 of U.S. Patent No. 6,432,445 in view of U.S. Patent No. 5,962,019. Applicants respectfully traverse the rejection and submit that claims 12-26 of the present application do not define an invention that is merely an obvious variation of the invention claimed in the '445 patent. None of the claims of the '445 patent suggest a pharmaceutical composition comprising polyethylene glycol. The Examiner has cited the '019 patent apparently to show that any variation between claims 12-26 of the present application and the claims of the '445 patent (e.g., PEG recited in the present claims), would have been obvious to one of skill in the art. The Examiner has not, however, shown that one skilled in the art would find it obvious to limit the compositions to be substantially free of any additional oil, i.e., wherein less than 5% of oils apart from those present in the surfactant, are present in the composition. In fact, the '019 patent would suggest to one skilled in the art that additional oils may be used. See '019 patent, column 4, lines 42-65 where specific fatty acids for use in the

compositions are enumerated. Thus, the presently pending claims do not recite obvious variants of the invention claimed in the '445 patent. Withdrawal of the nonstatutory obviousness-type double patenting rejection of claims 12-26 over claims 1-14 of U.S. Patent No. 6,767,445 in view of U.S. 5,962,019 is therefore warranted.

Claims12-26 have also been rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-14 of U.S. Patent No. 6,767,555 in view of U.S. Patent No. 5,962,019. Applicants respectfully traverse the rejection and submit that claims 12-26 of the present application do not define an invention that is merely an obvious variation of the invention claimed in the '555 patent. None of the claims of the '555 patent would suggest to one skilled in the art that the compositions be substantially free of any additional oil, i.e., wherein less than 5% of oils apart from those present in the surfactant, are present in the composition as presently claimed. In fact, claims 2, and 5-7 of the '555 patent in reciting a lipophilic surfactant and a lipophilic component, require additional oil to that of the compositions of presently pending claims 12-26. Further, the '019 patent at column 4, lines 42-65, would suggest to one skilled in the art that additional oils resulting in greater than 5% of oils apart from those present in the surfactant, may be used in the composition. Thus, the presently pending claims do not recite obvious variants of the invention claimed in the '555 patent. Withdrawal of the nonstatutory obviousness-type double patenting rejection of claims 12-26 over claims 1-14 of U.S. Patent No. 6,767,555 in view of U.S. 5,962,019 is therefore also warranted.

Claims 12-26 remain rejected under 35 U.S.C.§ 103(a) as allegedly unpatentable over U.S. Pat. No. 5,342,625 to Hauer et al. in view of U.S. Pat. No. 5,962,019 to Cho et al.

Hauer et al. has been cited for teaching cyclosporin pharmaceutical compositions in the form of micro-emulsion pre-concentrates that are filled in hard gelatin capsules. The abstract, examples, and column 29, lines 11-14 are specifically cited for this teaching.

At page 4 of the office action, the Examiner refers to columns 26-29 of Hauer et al., directed to a cyclosporin formulation which includes surfactants Cremophor RH40, which is described as a reaction product of hydrogenated or natural vegetable oil and ethylene glycol with an HLB value of 14-16. Therefore, the Examiner has taken the position that "the surfactant of Hauer meets the claimed surfactant component."

Applicants respectfully submit that in every example at columns 26-29 of Hauer et al., that employs Cremophor RH40, which according to the Examiner is a surfactant meeting Applicants' claims, the compositions also contain either Miglyol 812 or Myritol 318. *See e.g.,* compositions 1.2-3.11 of Examples 1-3 of Hauer et al. Miglyol 812 is a fractionated coconut oil comprising caprylic-capric acid triglycerides. Myritol 318 also comprises caprylic-capric acid triglycerides. *See* column 9 of Hauer et al. These examples therefore, comprise oil *in addition* to (b) a surfactant of HLB value of at least 10, comprising a reaction product of hydrogenated or natural vegetable oil and ethylene glycol. Applicants further submit that the amounts of oils used in Examples 1-3 of Hauer et al. are not insignificant. *See e.g.* Example 3: Miglyol 812 at 16.6% by weight; Example 1, composition 1.5: Myritol 318 present at 100 mg/capsule out of a quantity of total components: 855.0 mg/capsule. In contrast, presently amended claim 12 and claims 13-26, which depend or eventuate from claim 1, require that less than 5% of oils apart from those present in the surfactant, are present in the composition.

The Examiner has commented on the top of page 5 of the office action, paragraph 1, final sentence, that "Not all of the compositions of Hauer contain additional oils and the claimed lower alkanols." Applicants submit that Examples 4-7 of Hauer et

al. do not comprise additional oils. However, Examples 4-7 employ a C1-5 alkyl or tetrahydrofurfuryl di- or partial ether, e.g., (Transcutol or Glycofurol) which compounds are not required by the present claims. More importantly, the compositions in Examples 4-7 of Hauer et. al., do not contain a hydrophilic phase comprising a polyethylene glycol and at least one lower alkanol selected from ethanol and propylene glycol, as required by Applicants' claims 12-26.

Summarizing, in those instances in Hauer et al. where a surfactant of HLB value of at least 10 comprising a reaction product of natural or hydrogenated vegetable oil and ethylene glycol are present, and "therefore meet the claimed surfactant component" such compositions comprise additional oils. In contrast, the presently amended claims recite in addition to cyclosporin A, a surfactant and a hydrophilic phase, "wherein less than 5% of oils apart from those present in the surfactant, are present in the composition.

On page 5, line 5 of the office action, the Examiner readily admits that "Hauer fails to teach polyethylene glycol in combination with the lower alkanols." In order to fill the gap in teaching provided by Hauer et al., Cho et al. has been cited.

Cho et al. has been cited for teaching hard gelatine capsules comprising cyclosporin formulations comprising at least one alkanol solvent constituting an alkanol having 2 to 3 carbon atoms and a co-solvent selected from fatty acids and diols, including polyethylene glycols. According to the Examiner, Cho et al. teach incorporating at least one surfactant, such as polyoxyalkylene surfactant having an HLB value of 5 to 20 or preferably 8 to 16. Applicants submit that Column 3, lines 62-63 of Cho et al. specifically teach "Also present in the orally acceptable vehicle will be at least one non-ionic polyoxyalkylene surfactant, usually not more than two non-ionic polyoxyalkylene surfactants." In contrast, the present claims recite a surfactant which comprises a reaction product of a natural or hydrogenated vegetable oil and ethylene

glycol. There is no motivation or suggestion in Cho et al., to substitute a surfactant comprising a reaction product of natural or hydrogenated vegetable oil and ethylene glycol of Applicants claims for the non-ionic polyoxyalkylene surfactant taught by Cho et al.

At page 6, lines 3-6, of the office action, the Examiner posits that while Hauer et al. does describe oils, the examples of Hauer et al do not necessarily contain oils and "further instant specification does not define what "substantially free of oils" stands or the upper limit that meets the limitation." As discussed fully above, in every single example of Hauer et al., where a surfactant of HLB value of at least 10 comprising a reaction product of natural or hydrogenated vegetable oil and ethylene glycol are employed, the composition either contains additional oils (Examples 1-3) or else do not comprise a hydrophilic phase comprising a polyethylene glycol and at least one lower alkanol selected from ethanol and propylene glycol, wherein each lower alkanol present is present in an amount of less than 12% of the total weight of the composition disregarding the hard gelatine capsule, as required by Applicants' claims 12-26.

Further, as discussed above, claim 12 has been amended to recite in relevant part: "wherein less than 5% of oils apart from those present in the surfactant, are present in the composition" rather than "the composition being substantially free of any additional oil." Support for this amendment may be found throughout the specification, e.g., page 2, lines 10-11.

As fully discussed above, Hauer et al., in teaching compositions containing oils e.g., Miglyol 812, and Myritol 318, present in significant quantities in addition to a surfactant of HLB value of at least 10 comprising a reaction product of natural or hydrogenated vegetable oil and ethylene glycol, certainly do not suggest the presently claimed compositions, wherein less than 5% of oils apart from those present in the surfactant, are present in the composition. Cho et al. also do not suggest that a

cyclosporine a formulation should be substantially free of any additional oil, i.e. wherein less than 5% of oils apart from those present in the surfactant, are present in the composition. Cho et al. instead describe the further addition of fatty acids or fatty acid esters. *See* Cho et al., column 4, lines 29-65. *See especially* column 4, lines 60-65, where Cho et al. teach fatty acid esters present in an amount of at least equal (v/v) and up to 8 times the amount of surfactant in the formulation, usually not greater than 5 times the amount of the surfactant in the formulation (v/v).

Based on the foregoing, the specific combination of components of the hard gelatine capsules containing a pharmaceutical composition as presently claimed is not suggested by the combination of teachings provided by Hauer et al. in view of Cho et al. Withdrawal of the rejection of claims 12-26 under 35 U.S.C. §103(a) is therefore warranted.

Accordingly, in view of the foregoing remarks and amendments, it is respectfully submitted that the present claims are in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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